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COMPENSATORY RENAL HYPERTROPHY AND CHANGES OF RENAL FUNCTION FOLLOWING NEPHRECTOMY

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We studied the changes in the serum creatinine level and the volume of the remaining kidney following nephrectomy using contrast-enhanced compuded tomogram (CT) scans. Twenty-five patients undergoing nephrectomy for renal cell carcinoma without obvious disease in the remaining kidney were carefully followed for a period of at least two years at our hospial. Twelve patients received follow-up CT scans each year after nephrectomy. The ellipsoid volume of the kidney was calculated by measuring the 3-dimensional size on CT scans. The mean relative volume (%) of the remaining kidney increased up to year 3 postoperatively, and the final mean relative volume at varying periods from years 2 to 7 was 120%. Kidneys that were smaller prior to nephrectomy showed a tendency to have a larger final relative volume after nephrectomy, although there was no significant correlation between the kidney volume prior to nephrectomy and at final measurement. The mean serum creatinine level was significantly increased at one year after nephrectomy, but it decreased significantly over time. Therefore, both compensatory renal hypertrophy and improved renal function seemed to be established within several years after nephrectomy. However, the improvement of serum creatinine was delayed compared with the increase of kidney volume. That is, renal plasma flow might be increased early by compensatory renal hypertrophy, followed within a few years by an increase in glomerular filtration and a decrease of serum creatinine.

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Key words: Compensatory renal hypertrophy, Renal function, Nephrectomy, Renal cell carcinoma, Creatinine

INTRODUCTION

Postnephrectomy compensatory renal hypertrophy has been well documented both clinically[1–7] and experimentally[8,9]. This process involves both hypertrophy and proliferation of renal tubular cells[10] Angiotensin II, insulin-like growth factor-1, epidermal growth factor[10], and hepatocyte growth factor[11] have been reported to be involved in tubular hypertrophy. Postnephrectomy compensatory renal hypertrophy in animals is known to be complete within a short period[8,9] However, little is known about the time until completion of hypertrophy and improvement of renal function in adult humans[4,5] To assess the changes of the serum creatinine level and hypertrophy of the remaining kidney over time, we reviewed the data on serum creatinine and 3-dimensional renal size after contralateral nephrectomy in patients with renal cell carcinoma.

PATIENTS AND METHODS

Twenty-five patients were followed for at least 2 years at our hospital after nephrectomy for renal cell carcinoma between 1989 and 1996. None of them had any disease in the remaining kidney. Contrast-enhanced CT scans (5–10 mm slice interval) were taken before nephrectomy in all patients and almost every year after nephrectomy in 12 patients. Urinalysis and measurement of serum creatinine were repeated annually in all patients.

To calculate the volume of the remaining healthy kidney, we measured the longitudinal dimension (a), the maximum transverse dimension (b), and the maximum sagittal dimension (c) on CT scans, as

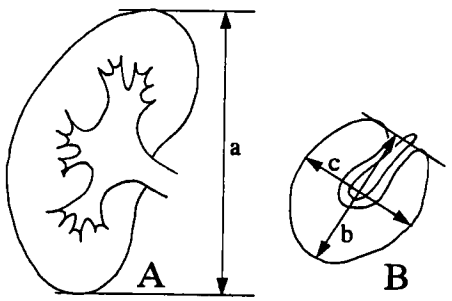

Fig. 1. Diagram of 3-dimensional CT measurement of the right kidney. The longitudinal dimension (a) is the distance between the upper and lower pole renal CT slices which include part of the kidney, as shown in A. The maximum transverse dimension (b) and sagittal dimension (C) are measured on renal CT scans, as shown in B.

Table 1. The remaining kidney volume (cm^3) calculated by measuring the 3-diamensional size on CT scans before and after contralateral nephrectomy

No.	Age	Sex	Post nephrectomy year							
			Pre	1st	2nd	3rd	4th	5th	6th	7hh
1	43	F	192	207	227					
2	45	F	225	225	225	225				
3	47	M	151	162	172	172	182	182		
4	49	F	181				198	198	190	
5	53	M	188	217	230	264				
6	54	M	219	224	235	243	243	243		
7	55	F	122	128	128	128	140	145	140	145
8	56	F	151	187	194	200				
9	59	M	239	243	243	249	249	243	249	249
10	62	M	171	225	225	236	228	257	236	236
11	65	F	186	228	236					
12	75	M	114	139	142	142				
Mean±SD			178±39	199±39**	205±40**	207±49**	207±42*	211±44*	204±49	210±57

Pre-=prenephrectomy, SD=standard deviation. *, **=significant (*: $p<0.05$, **: $p<0.01$) increase compared with the prenephrectomy kidney volume.

shown in Fig. 1. The longitudinal dimension was obtained from the number and the slice interval of the transverse CT scans which included part of the kidney. The kidney volume was calculated as an assumed elliposoid volume ($V=4/3\times\pi\times a/2\times b/2\times c/2$)[12]. The volume of the remaining kidney relative to its baseline volume (100%) was also calculated as follows: Relative volume = R2/R1×100, where R1 and R2 were the kidney volumes before and after surgery, respectively.

Serum creatinine, kidney volume, and relative kidney volume before and after nephrectomy were compared, separately for males and females, and patients older and younger than 60 years of age. Paired and unpaired data were tested by Students' *t*-test. Reselts are reported as the mean±standard deviation and $p<0.05$ was considered statistically significant.

RESULTS

The kidney volumes before and after nephrectomy are shown in Table 1. The mean relative volume of the remaining kidney was 113, 116% and 119% 1, 2 and 3 years after rephrectomy, respectively (Fig. 2). Thereafter, the mean relative volume showed no increase, and the mean final relative volume at varying periods from 2 to 7 years after nephrectomy remained at 120%. The mean relative volume of the remaining kidney was significantly different between baseline and 1 year ($p=0.0032$), and between 1 and 2 years ($p=0.0057$). However, there were no differences in the mean relative kidney volume between males and females ($p>0.1$) or between patients older and younger than 60 years of age ($p>0.1$). Kidneys that were smaller prior to nephrectomy tended to have a larger final relative volume after nephrectomy,

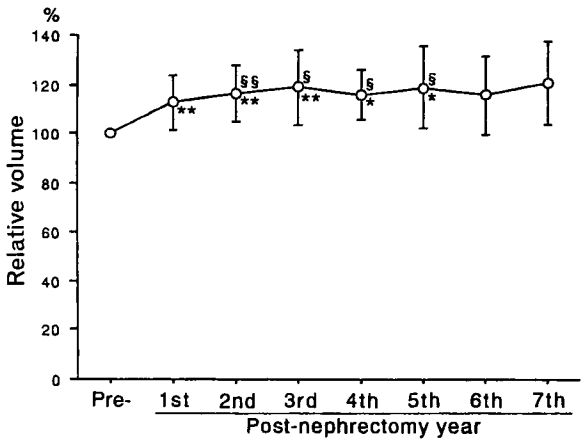

Fig. 2. Relative volume of the remaining kidney before and after contralateral nephrectomy in comparison with the prenephrectomy volume. Kidney volume increased up to 2 years after nephrectomy. Open circles and bars show the mean and standard deviation. Pre-= prenephrectomy. **, *=significant (**: $p<0.01$, *: $p<0.05$) increase compared with the prenephrectomy kidney volume. §§, §=significant (§§: $p<0.01$, §: $p<0.05$) increase compared with the relative kidney volume at 1 year.

although there was no significant correlation ($p=0.0955$) between the kidney volume prior to nephrectomy and at final measurement after 2 to 7 years (Fig. 3).

The mean serum creatinine was 0.98 mg/dl, at baseline; it rose significantly to 1.23 mg/dl after 1 year ($p<0.0001$), and stayed significantly higher up to 5 years relative to that at baseline ($p<0.05$) (Fig. 4). However, the mean serum creatinine decreased from 1 year onwards being significantly lower 2, 6, 7, and 8 years ($p<0.05$) compared with that 1 year after

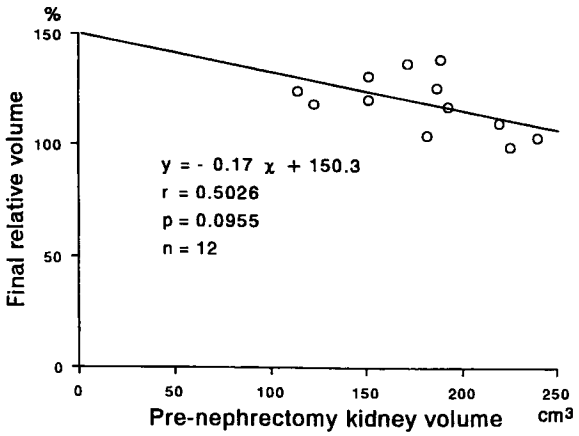

Fig. 3. Relationship between the prenephrectomy kidney volume and the final relative volume of the remaining kidney after contralateral nephrectomy. Prenephrectomy volume tended to be negatively correlated with the final relative volume of the remaining kidney.

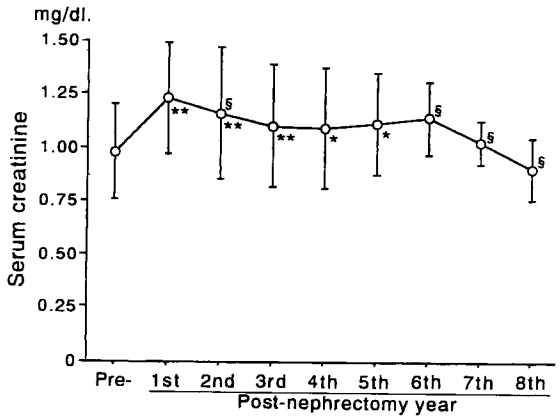

Fig. 4. Serum creatinine level before and after contralateral nephrectomy. Serum creatinine was higher from 1 (n=25) through 5 (n=10) years in comparison with the prenephrectomy level (n=25), but decreased from 1 year onwards, being significantly lower at 2 (n=20), 6 (n=7), 7 (n=5), and 8 (n=3) years compared with that at 1 year. Open circles and bars show the mean and standard deviation. Pre-=prenephrectomy. **, *=significant (**: $p<0.01$, *: $p<0.05$) increase compared with the prenephrectomy serum creatinine ilevel. §§, §=significant (§§: $p<0.01$, §: $p<0.05$) decrease compared with the serum creatinine level in 1 year.

nephrectomy. No patients developed proteinuria or hematuria after nephrectomy.

DISCUSSION

We demonstrated that compensatory renal hypertrophy and a compensatory increase in renal function were almost completed within a few years after nephrectomy. This change seemed to occur irrespective of gender or age. The baseline kidney volume tended to be negatively correlated with the final relative volume of the unresected kidney.

Renal hypertrophy has been assessed by various studies involving longitudinal measurements of the kidney on intravenous urograms[1-3], and by a few studies of the renal parenchymal volume on renal ultrasonograms[6,7] or CT scans[4,5] In this study, we measured the 3-dimensional kidney size on renal CT scans, and calculated the renal volume using the formula for an ellipsoid body[12]. With this method, the 3-dimensionally calculated volume of the prostate gland on ultrasonography has been shown to correlate well with the weight of the gland resected by prostatectomy[13] Longitudinal dimensions obtained in this study might be slightly shorter than the real lengths because of tilting of the renal axis and because judgement was based on the CT slice interval, the transverse and sagittal dimensions might be slightly longer than the true lengths. We only used contrast-enhanced CT scans for measurement because intravenous injection of contrast medium has been reported to expand the kidney size[14].

The mean relative increment in length of the unresected kidney in adult transplant donors[1] or in patients with renal disease[2] is reported to be 3.3–10.56% at several years after nephrectomy. In patients with renal carcinoma, Prassopoulos et al.[4] reported that the mean enlargement of the remaining kidney measured on CT scans was 15% at 3 months and 30% at 1 year after nephrectomy, but only 5% at 2.5 years after nephrectomy. Prassopoulos et al.[5] also reported that the remaining kidney was 36% larger at 1 month before nephrectomy, as well as 54% at 1 year, 62% at 2 years, and 47% at 3 years after nephrectomy in patients with renal carcinoma than the normal kidneys shown on CT scans of binephric individuals without renal disease. When the preoperative increase of kidney size (36%) was substrated from the overall hypertrophy (53%), they found 17% renal growth caused by nephrectomy. This postoperative renal growth (17%) is similar to our finding that the mean final relative increase was 20%. They also stated that the relative volume of the remaining kidney decreased at 2.5[4] or 3 years after nephrectomy[5]. In our study, although the remaining kidney volume decreased slightly or transiently decreased after nephrectomy in some patients, the mean volume did not fall significantly. Dossetor[2] studied compensatory renal hypertrophy in patients with renal tumors followed for up to 8 years after nephrectomy, and found that the relative longitudinal dimension of the remaining kidney showed no tendency to decrease, espesially in patients with longer follow-up. However, it appears obvious that compensatory renal hypertrophy occurs immediately after nephrectomy. Anderson et al.[15] have reported that the mean effective renal plasma

flow of the remaining kidney also increases by 32.5% at 1 week and by 30.1% at 1 year after donor nephrectomy. On the other hand, we found that serum creatinine increased at 1 year after nephrectomy and decreased again at 2 years after nephrectomy. Thus, there was discrepancy between the changes of kidney volume and serum creatinine after nephrectomy. Liu et al. have reported that the glomerular filtration rate was significantly lower in renal transplant donors whose mean follow-up period was 3.1 years than in patients with renal disease whose mean follow-up period was 18.8 years after nephrectomy[16]. Ter Wee et al. have also reported that glomerular filtration rate measured short term (1.3±0.3 months) after kidney donation amounted to 62±2.1% of the value before donation and to 68± 1.7% ($p<0.005$) of the value long term (4.9±0.8 years) after donation, and that short- and long-term effective renal plasma flow both amounted to 68% of the value before donation[17]. Because the serum creatinine level is related to the glomerular filtration rate and compensatory renal hypertrophy seems to be related to renal plasma flow, a significant increase of glomerular filtration is delayed a few years beyond the immediate increase of renal plasma flow after contralateral nephrectomy. In our study, the final relative increase of kidney volume at 2–7 years after nephrectomy was 20%. This increase may have been enough to keep the serum creatinine level similar to that before nephrectomy.

The mean relative kidney volume did not differ between males and females, or between patients over and under 60 years of age, in agreement with the results of Boner et al.[1], Ekelund and Gothlin[3], and Prassopoulos et al.[5] who have previously examined the relationship between renal hypertrophy and age or sex, although Anderson et al.[15] have reported that the effective renal plasma flow of the remaining kidney was significantly greater in male than in female patients after donor nephrectomy. In our study, smaller kidneys before nephrectomy tended to show a larger final relative volume after nephrectomy. The possible reasons were thought to be as follows : 1) a certain volume of kidney tissue might be needed to maintain a normal serum creatinine level, 2) larger kidneys before nephrectomy might have more functional reserve, or 3) larger kidneys before nephrectomy might already have undergone hypertrophy because the other kidney with renal cell carcinoma had lost most of its function[5]. The third one seems to be the most likely.

CONCLUSION

This study demonstrated that compensatory renal hypertrophy and a compensatory increase in renal function after nephrectomy are completed within several years. However, the recovery of serum creatinine is delayed in comparison with the increase in kidney volume. Contralateral renal plasma flow may increase immediately after nephrectomy, followed by a significant increase of the glomerular filtration rate within a few years. The gender and age of the patient does not appear to influence compensatory renal hypertrophy, but smaller kidneys prior to nephrectomy seem to enlarge more after nephrectomy. In contrast, larger kidneys seem to have already undergone hypertrophy prior to nephrectomy because the function of the contralateral kidney may often be impaired by involvement with renal cell carcinoma.

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和文抄録

腎摘除術後の対側腎の代償性肥大と腎機能の変移

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腎摘除術後の対側腎の体積と腎機能の変移を検討した．対象は腎細胞癌で腎摘除術を受け，対側腎に明らかな異常がなく，当院で少なくとも2年以上経過観察している25例であった．25例中12例で毎年CT検査を受けていた．腎の体積は造影CT上の腎の3方向の径を測定し楕円体体積の公式に当てはめて求めた。対側腎の体積は術後3年目まで増加し，術前体積（100%）に比べて2～7年後の平均最終体積は120%であった．対側腎の腎摘前の体積と術後の最終体積の間に有意な相関はなかったが，術前に小さい腎は腎摘後の最終体積比率が大きい傾向にあった．血清クレアチニン値は術後1年目に有意に増加したが，1年目の値に比べてその後数年の経過で有意に低下した．つまり，代償性腎肥大と腎機能の改善は術後数年以内に完成されるものの，腎肥大に比べて血清クレアチニン値の改善は遅れた．この理由として，術後早期の腎血漿流量の増加に伴って代償性腎肥大は起こるが，糸球体濾過率の上昇は2～3年遅れるため，上昇していた血清クレアチニン値の低下も遅れたことが考えられた．

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